U. S. Patent and Trademark Office
The Examiner
Patrick T. Lewis Ph D
Fax No:+571-273-~~8001~~ 8300

My Reference: Patent Application Number: 09/944,564

Date: October 10, 2006
Total number of pages: 8+ Filing Reciept
Annexes will be sent by mail

Fax letter

Response to Office Action dated 07/11/2006 (Final Rejection)
Notice of Appeal from the Examiner to the Board of Appeal and Interferences

Dear Sir:

In response to the above-identified final rejection of my patent application claims 25-27, may I kindly submit the following response:

1- By submitting a Notice of Appeal From the Examiner to the Board of Appeal and Interferences [Form: PTO/SB/31 (07-06)].
2- Payment by Credit Card. Form PTO-2038 is attached.
3- Objection to the Examiner decision by submitting further evidence from medical textbooks clarifying the point of dispute with the examiner; in relation to the definition of asthma and asthmatic bronchitis, and differentiating them as unrelated separate medical entities, thus rendering my claims in the use of glycophosphopeptical in the treatment of asthma patentable and valid.
4- Amendment of claim 25, currently reads as "25. (New) A pharmaceutical composition consisting essentially of glycophosphopeptical for oral administration for the treatment of **allergy** and **asthma** in dosage and duration which is effective to....etc"; may I kindly request separation of the use of glycophosphopeptical in the treatment of allergy from its use in the treatment of asthma. Discussion of the use in the treatment of allergy are part of the response to Office Action dated ....

Detailed response will follow.

Thank you for considering my appeal.

Best regards
N. Nadaim

The Inventor
Nida Nasif

Application/Control No.: 09/944,564 Page 1 Examiner: Patrick T. Lewis
Inventor: Nida Nassief Board of Appeal and Interferance

Notice of Appeal from the Examiner to the Board of Appeal and Interferences

Submitted in Response to Office Action dated 07/11/2006 (Final Rejection)

Date: October 10, 2006

Dear Sir:

Please fid following detailed response:

Rejection of Record Set Forth in the Office Action Dated November 21,2005

In this Office Action the Examiner have rejected claim 25 - 27 of my patent application number 09/944,564. Currently I am defending claim 25 that reads as follows:

25. (New) A pharmaceutical composition consisting essentially of glycophosphopeptical for oral administration for the treatment of **allergy** and **asthma** in dosage and duration which is effective to:

i- Switch-off the airway eosinophilic inflammation.
ii- Reduce mucus secretion.
iii- Reduce symptom score significantly.
iv- Restore airway patency as measured by Pulmonary Function Test.

The cause of rejection

From the above identified Office Action pages 3 - 4:

7. Claims 25-27 are rejected under 35 U. S. C. 102(b) as being anticipated by Sanchez Palacios A. et. al. Allergol Immunopathos (Madr) (1992), Vol 20 (1), pages 35-39 (Sanchez).

Sanchez discloses the use of Immunoferon (AM3) in the treatment of childhood infectious respiratory pathology. To assess the immunoclinical effectiveness of a biologic response immunomodulator, glycophosphopeptide (AM3) was administered to 20 children with asthmatic bronchitis. The children received 2 envelops (1gm) daily for 4 months. The clinical and immunological parameters assessed were: cough, dyspnoea, expectoration, frequency and intensity of bronchospasm, time of administration of the symptomatic medication, and the delayed cutaneious cells response by means of the intradermal reaction of 5 antigens: Immunoferon reduced the symptoms, the intensity and frequency of the bronchospasm, and the symptomatic medication.

8. Aplicant's argument filed April 12, 2006 has been fully considered but they are not persuasive. Applicant's argue that Sanchez is referring to infectious respiratory pathology (asthmatic bronchitis) which is not bronchial asthma which is allergic or atopic.

Applicant's arguments have been considered but are not deemed germane. Sanchez teaches the use of glycophosphopeptide for treating asthmatic bronchitis. It was well known in the art at the time of the invention that asthmatic bronchitis is a condition in which the airways in the lung are obstructed due to both persistent asthma and bronchitis. Thus, the patient population treated by the method of Sanchez embraces asthma patients and therefore meets the limitation of the instantly claimed invention.

Appeal From the Examiner to the Board of Appeal and Interferences

What is my dispute difference of opinion) with the Examiner in relation to Office Action dated 07/11/2006

In this appeal, may I kindly request the Board of Appeal to consider the following two requests:

First: I am still arguing that asthma and asthmatic bronchitis are two separate unrelated diseases and that my claim rejection was brought up by confusion in the name between the old term of asthmatic bronchitis and asthma. Accordingly the use of glycophosphopeptical in the treatment of asthma in my patent is novel and kindly requesting its allowance.

Second: Claim 25 reads as "A pharmaceutical composition consisting essentially of glycophosphopeptical for oral administration for the treatment of allergy and asthma ....etc", I am arguing that the pharmaceutical composition for the treatment of "allergy" as a group of diseases referred to separately in the patent application, under description of the invention, with enabelment and previous clarification in my reply to the Office Action filed on Aug 2004 with X-ray films clarifying its unique outcome of early clinical testing , and will be detailed later, have been forgotten and overlooked. May I kindly request the allowance of this claimed invention.

In this reply, references to the standard teaching of medical textbooks are made for detailed description of asthmatic bronchitis. Selected chapters are photocopied, and the relevant paragraphs are underlined in order to clarify the source of confusion in the name, the differentiating clinical features, and the correlation between asthmatic bronchitis and asthma. I am trying to keep the text minimal, but excuse me for placing some paragraphs and sentences of secondary importance to keep the continuity of the reply.

Asthma is currently an international enigma with increasing incidence and uncontrolled patients. According to medical reports released during 2006 from the "Global Initiative Of Asthma" that will be included in the mail copy of this Response and Appeal.

Detailed Appeal / First

Claim 25 in relation to "A pharmaceutical composition consisting essentially of glycophosphopeptical for oral administration for the treatment of asthma"

My argument filed April 12, 2006 was that the Sanchez had excluded cases of asthma in patients selection as described in page 36 column 1 of the article as follows:

"MATERIAL Y METODOS

Pacientes. Se seleccionaron 40 ninos **no atopicos** con clinica respirotoria infecciosa de bronquuitis espastica y/o asmatica con pruebas **cutaneas a neumoallergenos negative** e **IgE total normal.**

May I **add** to my argument filed April 12, 2006 that referring to the title of the article by Sanchez which reads as " Valoracion clinica immunologica de un modificador de la respuesta biologica, AM3, en el tratamiento de la **patologia respiratoria infectiosa infantile"**, this description fits the condition of asthmatic bronchitis "bronchiolitis" as will follow, but not asthma.

In the Examiners Office Action dated 07/11/2006, page 4, line 7, he have the following comment "It was well known in the art at the time of the invention that asthmatic bronchitis is a condition in which the airways in the lungs are obstructed due to both persistent asthma and bronchitis." **My reply** is that "The term bronchiolitis was first used by Engle and Newns in 1940, bronchiolitis appears to have been born from a long lineage of confusing sobriquets, including "asthmatic bronchitis." As will be described below under the title "Bronchiolitis" page 5 of this report. Therefore at the time of filing my invention it was well known that asthma and asthmatic bronchitis are two separate diseases.

Most important, to support my argument further, I am submitting new evidence from the standard teaching of medical textbooks that clarifies the point that asthma previously was used to indicate "shortness of breath" as in the case of the term "**cardiac asthma**" that is used to denote shortness of breath in heart failure (Annex II). Furthermore the correlation between asthma and asthmatic bronchitis; selected from the textbook of Principles and Practice of Infectious Diseases 2005 (Annex III), asthmatic bronchitis is currently named bronchiolitis. The term bronchiolitis was first used by Engle and Newns in 1940 for the lower respiratory tract disease observed in young infants. The term bronchiolitis appears to have been born from a long lineage of confusing sobriquets, including "acute catarrhal bronchitis," "interstitial bronchopneumonia," "spastic bronchopneumonia," "capillary or obstructive bronchiolitis," and "asthmatic bronchitis." And that "We are dealing with two separate diseases that may coexist in an infant, and that children with bronchiolitis in infancy have no increased risk of asthma by the time they reach adolescence." This will be detailed further in the following text. May I kindly request consideration of this new evidence and other reference in the text and allow my claimed invention.

Confusing medical terms using asthma

The term asthma, historically, is used to designate any disease characterized by "asthma-like symptoms", in patients complaining of dyspnoea, wheeze, cough and sputum. Those diseases are unrelated to the disease entity of current asthma; examples are 1- "cardiac asthma" and 2- "asthmatic bronchitis".

1- Cardiac Asthma

The clinical manifestations of heart failure includes respiratory disturbances as dyspnoea and paroxysmal nocturnal dyspnoea; this term refers to attacks of sever shortness of breath and coughing that generally occur at night. Cardiac asthma is closely related to paroxysmal nocturnal dyspnoea and nocturnal cough and is characterized by wheezing secondary to bronchospasm-most prominent at night.

Annex II - Part VIII Disorders of the Cardiovascular System: page 1370. HARRISON'S PRINCIPLES OF INTERNAL MEDICINE. 16th Edition (2005) Mc Graw-Hill

2- **Bronchiolitis (Asthmatic Bronchitis)**

Exact definition of asthmatic bronchitis is available from a textbook of "Principles and Practice of Infectious Diseases", selected paragraphs follows indicates that we are dealing with two separate diseases that may coexist in an infant, The following statements contitute a reply to the point raised by the examiner::

Page 812, coloumn 2: "Bronchiolitis is an acute viral lower respiratory tract illness that occurs during the first 2 years of life. **The illness also has been called "wheezy bronchitis" and "asthmatic bronchitis". Whatever term is applied, the syndrome is caused primarily by viral infections. The characteristic clinical manifestations include an acute onset of wheezing and hyperinflation, most commonly associated with cough,** rhinorrhea, tachypnoea (increased respiratory rate) and respiratory distress."

"The term bronchiolitis appears to have been born from a long lineage of confusing sobriquets, including "acute catarrhal bronchitis," "interstitial bronchopneumonia," "spastic bronchopneumonia," "capillary or obstructive bronchiolitis," and "asthmatic bronchitis." Bronchiolitis, however, did not become recognized as a distinct entity until the 1940s."

In page 814, coloumn 1 under the term Pathophysiology **"The term bronchiolitis was first used by Engle and Newns in 1940** for the lower respiratory tract disease observed in young infants that tend to be sever and often fatal. The virus initially replicates in the epithelium of the upper respiratory tract, but in the young infant it tend to spread rapidly to the lower tract airways."

"Inflammatory changes of various severity are observed in most small bronchi and bronchioles. The inflammation and edema make the small-lumen airways in infants particularly vulnerable to obstruction. Thus, although airflow is impended during both inspiration and expiration, the latter is more affected and prolonged."

In the first column, last paragraph in page 815, under the title of "Pathophysiology": "Clarifying the relationship between bronchiolitis and subsequent asthma is complicated by confusion about the Pathophysiology of asthma itself".....Nevertheless, **"The association between bronchiolitis and asthma is not straightforward. Several investigatorshave demonstrated that children with bronchiolitis in infancy have no increased risk for asthma** or abnormal pulmonary function by the time they reach early adolescence.

In the first column of page 816 under the title "Diagnosis" and its continuation in the second column in the same page: "The diagnosis of bronchiolitis is made most frequently on the basis of the characteristic clinical and epidemiological findings. However considerable confusions exist over the exact definition of bronchiolitis. A variety of entities may cause a similar picture of dyspnoea and wheezing in the infant. Asthma is not easily differentiated, particularly if it is the infant's first episode. **Furthermore the two diseases may be combined."**

Annex III. Caroline Breese Hall and John T. McBride. Bronchiolitis. Chapter 60: 812-819. PRINCIPLES AND PRACTICE OF INFECTIOUS DISEASES. Sixth Edition 2005. Elsevier Churchill Livingstone.

Asthma – selected paragraphs related to my invention

The problem is related to the diseases manifested clinically by the triad of cough dyspnoea and wheeze.

Definition: Asthma is defined as a chronic inflammatory disease of the airways of any age. The symptoms of asthma consist of a triad of dyspnoea (shortness of breath), cough, and wheezing (respiration becomes audibly harsh and expiration becomes prolonged). The end of an episode is frequently marked by a cough that produces thick stringy mucus, when examined microscopically, often shows eosinophils (P1511). Asthma is an episodic disease, with acute exacerbations interspaced with symptom-free periods. Typically most attacks are lasting minutes to hours spontaneously or after treatment (P1508). The eosinophil appears to play an important part in the infiltrative component (P1509).

Stimuli that incite asthma (provoke acute episode) can be grouped into seven major categories (P1509):

- Allergens in allergic asthma (25-35% of all cases, young age up to 30 years) is dependant on an IgE response controlled by T and B lymphocytes and activated by interaction of antigen with mast cell-bound IgE molecule, mostly inhaled antigens (as pollens, dust, dust mite, cat dander, grasses ... ect).
- pharmacologic,
- environmental,
- occupational,
- infectious: respiratory infections are the most common of the stimuli that evoke acute exacerbation of asthma.
- exercise-related, and
- emotional

Differential Diagnosis of asthma (P1511)

The differentiation of asthma from other diseases associated with dyspnoea and wheezing is usually not difficult, particularly if the patient is seen during an acute episode. The physical findings, symptoms and the history of periodic attacks are quite characteristic. A personal and family history of allergic diseases such as eczema, rhinitis, or urticaria is valuable contributory evidence. An extremely common feature of asthma is nocturnal awakening with dyspnoea that its absence raises doubt about the diagnosis.

Upper airway obstruction by tumor or laryngeal edema can occasionally be confused with asthma. Asthma-like symptoms have been described in patients with glottic dysfunction, endobronchial disease as foreign body, heart (left ventricular) failure, carcinoid tumor, and chronic bronchitis ....etc. In chronic bronchitis there are no true symptom-free periods, and one can usually obtain a history of chronic cough and sputum production as a background on which acute attacks of wheezing are superimposed.

Annex I- McFadden Jr. E. R. Asthma. Section 2; Diseases of the Respiratory System: pages 1508-1512. HARRISON'S PRINCIPLES OF INTERNAL MEDICINE. 16th Edition (2005): 1508-1516. Mc Graw-Hill.

Detailed Appeal / Second

Claim 25 in relation to "A pharmaceutical composition consisting essentially of glycophosphopeptical for oral administration for the treatment of allergy"

Claim 25 reads as "A pharmaceutical composition consisting essentially of glycophosphopeptical for oral administration for the treatment of allergy and asthma ....etc", I am arguing that the pharmaceutical composition for the treatment of "allergy" as a group of diseases referred to separately in the patent application, under description of the invention, with enabelment and previous clarification in my reply to the Office Action filed on Aug 2004 with X-ray films clarifying its unique outcome of early clinical testing , and will be detailed later, have been forgotten and overlooked. May I kindly request the allowance of this claimed invention.

Please find my Reply filed Aug 2004, particularly page 2B last paragraph "Current allergic rhinitis medications till page 6B.

I will also include in the mail copy of this Response and Appeal additional updated references related to the same subject.

Other points raised by the Examiner in this Office Action

Election/Restriction

1. Applicant's election with traverse Group I in the reply filed on Aug 4, 2004 is acknowledged.

2. Claims 28-34 are withdrawn as being withdrawn to a non elected invention:

Reply: Agree

Information Disclosure Statement

3. The listing or citing of references in applicant's response is not a proper information disclosure statement.

Applicant's Response Dated April 12, 2006

4. Claims 25-34 are pending. Claims 28-34 are withdrawn from further consideration as being drawn on nonelected invention. An action on the merit of claims 25-27 is considered herein below.

5. The rejection of claims 25-27 under 35 U. S. C. 102(b) as being anticipated by Sanchez Palacios A. et. Al. is maintained for the reasons of record as set forth in the Office Action dated November 21, 2005.

Thank you for your consideration
The Inventor
Nida Nassief

END OF REPORT
X Ray Follows

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P8

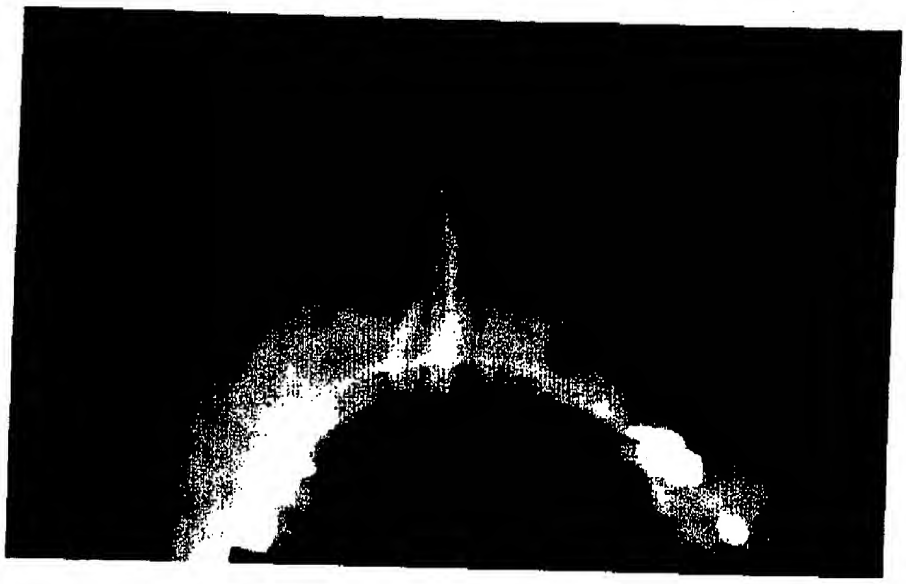

Figure 1: Photographs of X-ray Paranasal sinuses (PNS) of a 42 years old male patient, with a 15 years history of allergic rhino-sinusitis. Figure 1: X-ray PNS shows thickening of the mucosal lining of the right maxillary antrum and bilateral hypertrophy of nasal turbinates, patient treated by conventional therapy.

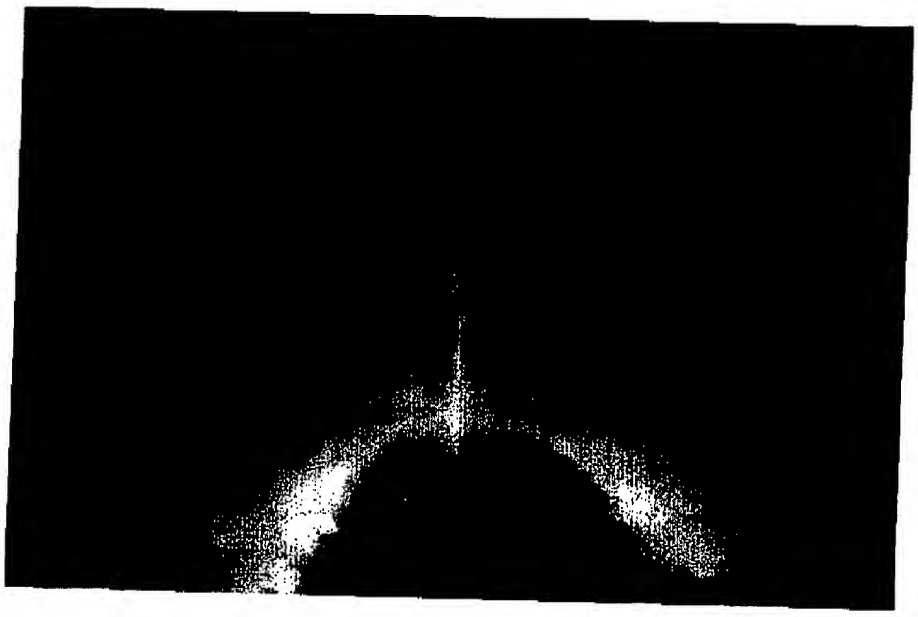

Figure 2: same patient, 5 months after treatment with 2 courses of immunoferon therapy, showing very good resolution of the mucosal thickening of the right maxillary antrum, better aeration of the nasal cavity and mild-moderate resolution of the turbinate hypertrophy.